

Appl. No. 09/284,009

PATENT

Supplemental Response under 37 C.F.R. § 1.111

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

LISTING OF CLAIMS:

Claims 1-86 (canceled)

87. (Previously presented) A mononuclear phagocyte modified to comprise at least one regulatable element operably linked to at least one nucleotide sequence of interest (NOI), wherein said regulatable element is selected from a hypoxia regulatable element, an ischemic regulatable element and a stress regulatable element.

88. (Previously presented) The mononuclear phagocyte according to claim 87 wherein expression of the NOI is regulated by the regulatable element at a target site selected from the group consisting of an hypoxic site, an ischemic site, a stress site, and a site being a combination of at least two of an hypoxic site, and ischemic site, and a stress site.

89. (Previously presented) The mononuclear phagocyte according to claim 87 or claim 88 wherein the mononuclear phagocyte further comprises a binding agent capable of binding to a cell surface element of the mononuclear phagocyte.

90. (Previously presented) The mononuclear phagocyte according to claim 89 wherein the binding agent comprises a mannosylated poly — L — lysine ligand.

91. (Previously presented) The mononuclear phagocyte according to claim 89 wherein the binding agent comprises a viral vector for internalising the regulatable agent into the mononuclear phagocyte.

92. (Previously presented) The mononuclear phagocyte according to claim 87 wherein the NOI is incorporated into the genome of the mononuclear phagocyte.

93. (Previously presented) The mononuclear phagocyte according to claim 91 wherein the viral vector is a lentiviral vector.

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Claims 94-100 (canceled).

101. (Previously presented) The mononuclear phagocyte according to claim 87 wherein the mononuclear phagocyte further comprises an NOI encoding HIF1-alpha or a tetracycline repressor protein.

Claims 102-103 (canceled).

104. (Currently amended) The mononuclear phagocyte according to claim 87 wherein the ~~mononuclear phagocyte further comprises an~~ at least one NOI encodes a pro-drug activation enzyme encoding a protein that kills mononuclear phagocytes.

Claims 105-108 (canceled).

109. (Currently amended) A delivery system for targeting a mononuclear phagocyte ~~according to claim 87~~ to a target site, said system comprising the mononuclear phagocyte according to claim 87 and a binding agent capable of binding to a cell surface element of the mononuclear phagocyte, wherein the target site is selected from the group consisting of an hypoxic site, an ischemic site, a stress site, and a site being a combination of at least two of an hypoxic site, an ischemic site, and a stress site.

110. (Currently amended) The mononuclear phagocyte according to claim ~~[[87]]~~ 88 wherein the hypoxic, ischemic or stress site is a target site of a tumor associated condition.

111. (Previously presented) A construct comprising at least one regulatable element operably linked to at least one nucleotide sequence of interest (NOI), wherein said regulatable element is selected from a hypoxia regulatable element, an ischemic regulatable element and a stress regulatable element, and wherein the construct is coupled to a binding agent that is capable of binding to a cell surface element of a mononuclear phagocyte.

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112. (Previously presented) The construct according to claim 111 wherein the regulatable element is an HRE element.

113. (Previously presented) The construct according to claim 111 or claim 112 wherein the binding agent comprises a ligand adapted to bind to the cell surface element.

114. (Previously presented) The construct according to claim 111 or claim 112 wherein the binding agent comprises a viral vector for internalising the regulatable element into a mononuclear phagocyte.

115. (Previously presented) The construct according to claim 114 wherein the viral vector is selected from the group consisting of an adenoviral vector and a lentiviral vector.

116. (Previously presented) A method for internalising a regulatable element into a mononuclear phagocyte wherein the regulatable element is selected from a hypoxia regulatable element, an ischemic regulatable element and a stress regulatable element and the method comprises:

providing a mononuclear phagocyte; and

exposing the mononuclear phagocyte to a construct as defined in any one of claims 111 or 112 under conditions sufficient to internalise the construct into the mononuclear phagocyte.

Claims 117-119 (canceled).

120. (Previously presented) A pharmaceutical composition comprising a mononuclear phagocyte according to claim 87 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

121. (Previously presented) A pharmaceutical composition comprising a construct according to claim 111 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

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122. (Previously presented) A mononuclear phagocyte comprising an NOI encoding a p450 enzyme wherein the NOI has been internalised into the mononuclear phagocyte by an adenoviral vector; and wherein the NOI encoding the p450 enzyme is operably linked to

a hypoxia response element (HRE); such that the p450 enzyme is expressed under conditions that occur either artificially by induction or occur/exist naturally.

123. (Currently amended) The mononuclear phagocyte according to claim [[96]] 104 wherein the pro- drug activation enzyme is a p450 enzyme.

124. (Previously presented) The mononuclear phagocyte according to claim 123 wherein the p450 enzyme, is a CYP2B6 p450 enzyme.

125. (Previously presented) The construct according to claim 113 wherein the ligand is a mannosylated poly — L — lysine.